the [N_2O_2] group is covalently bonded in said polymeric composition through said organic moiety X.

REMARKS

The Present Invention

The present invention is directed to polymeric compositions capable of releasing nitric oxide. The compositions comprise a biopolymer and a nitric oxide-releasing $N_2O_2^-$ functional group. The present invention is also directed to pharmaceutical compositions comprising such polymeric compositions and methods of treating biological disorders in a mammal in which dosage with nitric oxide is therapeutic.

The Amendment to the Claims

Claim 1 has been amended to point out more particularly and distinctly claim the subject matter of the present invention. No new matter has been added by way of this amendment.

The Pending Claims

Claims 1, 5-15, 19-27 and 31-38 are currently pending. Claims 1 and 5-14 are directed to polymeric compositions. Claims 15 and 19-26 are directed to pharmaceutical compositions. Claims 27 and 31-38 are directed to the method of treating biological disorders in a mammal.

The Office Action

The Office set forth the following rejections:

(i) claims 1, 5-15, 19-27 and 31-38 were rejected under 35 U.S.C. § 112, second paragraph; and

(ii) claims 1, 5-15, 19-27 and 31-38 were rejected as comprising an improper Markush group.

Reconsideration of these rejections is hereby requested.

Discussion of Rejection
under 35 U.S.C. § 112, second paragraph

The Office has rejected claims 1, 5-15, 19-27 and 31-38 under Section 112, second paragraph. Specifically, citing the language at the bottom of page 28 of the specification, the Office contends that the claims are not limited to polymers containing a peptide linkage

through which the polymer is covalently bonded to a nitric oxide functional group as exemplified in the specification. This rejection is traversed for reasons set forth below.

The specification clearly states that the $N_2O_2^-$ functional groups are "bound to the polymer." "Bound to the polymer" is defined as associated with, part of, incorporated with or contained within the polymer physically or chemically. Bonding of the $N_2O_2^-$ functional group to the polymer can be achieved by covalent bonding of the $N_2O_2^-$ group to the polymer directly or by covalent bonding of the $N_2O_2^-$ group to the polymer through a linking group X or X'. Chemical bonding of the $N_2O_2^-$ functional group to the polymer can be by, for example, covalent bonding of the linking group X or X' to the polymer such that the linking group forms part of the polymer itself, i.e., is in the polymer backbone, or is attached to a pendant group on the polymer backbone. The specification further states that the manner in which the nitric oxide-releasing $N_2O_2^-$ functional group is associated with, part of, incorporated with or contained within, i.e., "bound," to the polymer, is inconsequential to the present invention and all means of association, incorporation and bonding are contemplated (see, for example, page 6, line 18, through page 7, line 10, page 15, line 30, through page 17, line 12, page 19, line 17, through page 20, line 21, and the Examples).

Furthermore, Applicants have exemplified the preparation of the bis(nitric oxide) adduct of L-prolyl-L-leucylglycinamide in Example IV, the attachment of a nucleophilic center to a protein that does not contain a nucleophilic center that will readily react with NO in Example V, and the attachment of a preformed NONOate containing a nucleophilic nitrogen atom to the C-terminus of a peptide, polypeptide or protein in Example VI. In this regard, Applicants point out that, while the Office has honed in on Example VI, thereby ignoring Applicants demonstrations in Examples IV and V, it is not necessary, nor is it required, for Applicants to exemplify each and every embodiment encompassed by the claims. This is especially true in view of the fact that, as pointed out above and as set forth in the specification at, for example, page 15, line 30, through page 17, line 12, the manner in which the nitric oxide-releasing $N_2O_2^-$ functional group is associated with, part of, incorporated with or contained within, i.e., "bound," to the polymer, is inconsequential to the present invention and all means of association, incorporation and bonding are contemplated. In this regard, Applicants also point out that the Examiner has allowed claims directed to or involving the use of polymeric diazeniumdiolates. See, for example, U.S. Patent Nos. 5,405,919 (see, e.g., claim 1), 5,650,447 (see, e.g., claims 39 and 40), 5,718,892 (see, e.g., claim 1), and 5,676,963 (see, e.g., claims 1, 8 and 12).

In view of the above, Applicants submit that limitation of the claims to polymers containing a peptide linkage through which the polymer is covalently bonded to a nitric oxide functional group would unduly limit the scope of Applicants' invention. This is underscored

by Applicants' teaching in the specification that the manner in which the nitric oxide-releasing $N_2O_2^-$ functional group is associated with, part of, incorporated with or contained within, i.e., "bound," to the polymer, is inconsequential to the present invention. Accordingly, Applicants request withdrawal of this rejection.

Discussion of Markush Rejection

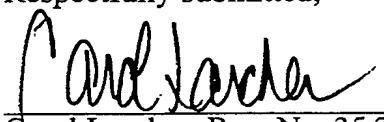
The Office has rejected claims 1, 5-15, 19-27 and 31-38 as comprising improper Markush groups. The Office contends that the claims define polymeric products in which the polymers have physical and chemical structures that would be the subject of separate areas of investigation and experimentation and are useful for diverse purposes. More specifically, the Office contends that nucleic acid, hormone and anti-chemotactic agent are not definite chemical structures and are unobvious from one another, when considered as possible equivalent compounds to be derivatized. This rejection is traversed.

Applicants submit that the claims do not comprise improper Markush groups because all of the polymeric compositions encompassed by any given claim comprise a biopolymer and at least one nitric oxide-releasing $N_2O_2^-$ functional group. As set forth in the M.P.E.P. at § 2173.05(h), "when the Markush group occurs in a claim reciting ....a combination (not a single compound), it is sufficient if the members of the group are disclosed in the specification to possess at least one property in common which is mainly responsible for their function in the claimed relationship, and it is very clear from their very nature or from the prior art that all of them possess this property." While the biopolymeric component of the claimed polymeric compositions can vary in physical or chemical structure and each of the recited biopolymers can be useful for diverse purposes, variability in physical or chemical structure and usefulness is irrelevant to the determination of the propriety of the Markush group of the claims because all of the claimed compositions are characterized by one common property that is mainly responsible for their function, i.e., the release of nitric oxide. Likewise, the contention that the chemical structures of the biopolymers "nucleic acid," "hormone" and "anti-chemotactic agent" are not defined in the claims and the contention that these biopolymers are unobvious with respect to one another in terms of their derivatizations are also irrelevant to the assessment of whether or not a given Markush group is proper. The group meets the letter of a Markush definition because each member of the group is disclosed in the specification to possess the common property of releasing nitric oxide, i.e., the property that is mainly responsible for the group's function in accordance with M.P.E.P. § 2173.05(h). Based on the above reasons, Applicants submit that the Markush group is proper and request withdrawal of this rejection.

Conclusion

In view of the above remarks, the application is considered to be in good and proper form for allowance and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of this application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,



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Date: July 31, 1998

In re Appln. of Saavedra et al.
Serial No. 08/837,812

CERTIFICATE OF MAILING

I hereby certify that this AMENDMENT AFTER FINAL REJECTION (along with any documents referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.

Date: July 31, 1998

THE PATENT AND TRADEMARK OFFICE IS RESPECTFULLY REQUESTED TO PLACE ITS STAMP ON THIS POSTAL CARD AND PLACE IT IN THE OUTGOING MAIL TO SHOW THE FOLLOWING PAPERS HAVE BEEN RECEIVED.

In re Application of Saavedra et al.
"Biopolymer-Bound Nitric Oxide-Releasing Compositions, Pharmaceutical Compositions Incorporating Same and Methods of Treating Biological Disorders Using Same"

Atty. Docket: 61192

Serial No.: 08/837,812

Filed: July 31, 1998

1. Transmittal Letter (1 pg.) in duplicate;
2. Amendment After Final Rejection with Certificate of Mailing (6 pgs.); and
3. Return Postcard.

Date Mailed: July 31, 1998

CLL:jda

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